DETAILED ACTION

RE: Garrett et al.

1. Applicant's species election of "ErbB2 amino acid residues 247-268 or a subset thereof" in the reply filed on 5/1/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Applicants request eventual examination of the entire claim is acknowledged.

3. Claims 47-64 are pending. Claims 1-46 have been cancelled. Claims 47-62 are withdrawn from further consideration as being drawn to non-elected inventions.

4. Claims 63 and 64 are under examination. Due to species election, claims are examined to the extent that the antibody is the one that binds to the amino residues 247-268 of ErbB2, or a subset thereof.

Priority

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

6. The information disclosure statements (IDS) filed on 4/1/2005 and 3/13/2006 have been considered. Signed copies are attached hereto.

Specification

7. The disclosure is objected to because of the following informality. The Brief Description of the Drawings mentions Figure 1 (A) and (B). However, Figure 1 in Drawing does not have (A) and (B). Correction is required.

Claim Objections

8. Claim 64 is objected to for reciting specific amino acid residues, for example, the residues 247-268 of ErbB2, because it is unclear which amino acid of ErbB2 is counted as residue 1. The specification teaches the human ErbB2 has 1234 residues (see page 2, lines 4-5), and the residue one appears to be Ser (see SEQ ID NO.1). However, Huston et al. (US Patent No. 5,877,305, Date of Patent: 3/2/1999) teach that the ErbB2 has 1255 residues, and the residue one is Met (see SEQ ID NO.2). The amino acid sequence of the residues 247-268 of instant SEQ ID NO.1 is different from the residues 247-268 of ErbB2 of Huston et al. As such, it is unclear what amino acid residues applicants intend to claim.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 63-64 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter

Claims 63-64, as written, do not sufficiently distinguish over antibodies as they exists naturally because claims do not particularly point out any non-naturally occurring differences between the claimed antibodies and the naturally occurring antibodies. In the absence of the hand of man, the naturally occurring antibodies are considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1966)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F.Supp 68 (1967), 155 USPQ 139, (District Court, New Jersey, 1967)). Amendment of the claims to recite "an isolated" or "purified" antibody or similar language would obviate this rejection.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 63 and 64 are rejected under 35 U.S.C. 102(b) as being anticipated by Godowski et al. (US 5,766,863, Date of Patent 6/16/1998), as evidenced by Cruse et al. (Illustrated Dictionary of Immunology, 1995 by CRC press, page 241).

Godowski et al. teach a polyclonal anti-HER2 antibody isolated from pooled immune sera from rabbits immunized with the extracellular domain of the HER2 (also called ErbB2) molecule (see column 33, lines 11-15). The anti-HER2 polyclonal antibody would comprise an antibody that binds to the residues 247-268 of HER2 or a subset thereof, as evidenced by Cruse et al. Cruse et al. teach that polyclonal antibodies are multiple immunoglobulins responding to different epitopes on an antigen molecule. Cruse et al. teach that this multiple stimulation leads to the expansion of several antibody-forming clones whose products represent a mixture of immunoglobulins in contrast to proliferation of a single clone which would yield a homogeneous monoclonal antibody product (see page 241, right column). Therefore, the antibodies of Godowski et al. read on the claimed antibodies.

13. Claims 63 and 64 are rejected under 35 U.S.C. 102(e) as being anticipated Sliwkowski (US Patent No. 6,949,245B1, Date of Patent: 9/27/2005, earliest effective filing date: 6/25/1999), as evidenced by Agus et al. (J. Clin. Oncol., 2005, 23(11): 2534-2543).

Sliwkowski teaches 2C4 antibodies which bind to amino acid residues 22-584 of ErbB2 (see Figure 1B). Sliwkowski teaches that 2C4 epitope of ErbB2 may be any one or more residues in the region from about residue 22 to about residue 584 of ErbB2

(see column 16, lines 44-46). Sliwkowski teaches antibodies that have a biological characteristic of a monoclonal antibody 2C4, such as bind the same epitope in the extracellular domain of ErbB2 as that bound by 2C4 (e.g. which blocks binding of monoclonal antibody 2C4 to ErbB2) (see column 4, lines 6-15, and column 14, lines 42-67). Sliwkowski teaches that these antibodies are capable of blocking HRG activation of ErbB2/ErbB3 (see column 14, lines 32-35). The antibodies of Sliwkowski bind to the CR1 domain (also called Domain II) dimerization loop as evidenced by Agus et al. Agus et al. teach that 2C4 antibody binds to HER2, at the dimerization domain, sterically inhibiting its ability to form dimmers with other HER receptors and the binding site is within domain II (see page 2635, 1st column, 3rd paragraph). As such the antibodies of Sliwkowski anticipate the instant antibodies.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kaumaya et al. (US 7,060,284B1, Date of Patent: 6/13/2006, earliest effective filing date: 8/3/1999).

For this rejection, the residues 247-268 of ErbB2 is interpreted as the residues 247-268 of SEQ ID NO.1 provided in the instant sequence listing (see paragraph 10 above).

Kaumaya et al. teach HER-2 B cell epitopes including SEQ ID NO.5 (see column 2, lines 41-61). The amino acid sequence of SEQ ID NO.5 is 100% identical to the instant residues 249-266 of SEQ ID NO.1 (see sequence alignment Exhibit A). Kaumaya et al. teach that the HER2 B cell epitopes have the ability to induce production of antibodies which are immunoreactive with the extracellular domain of the HER2 protein (see column 2, lines 62-65). Kaumaya et al. teach making antibodies using HER-2 B cell epitopes by immunizing animals with HER-2 B cell epitopes and purifying the antibodies from sera of the animals (see column 15, lines 18-39). Kaumaya et al. teach assaying the effect of Abs on cell proliferation (see column 16, line 51, column 20, lines 48-67, and column 21, lines 4-14).

While Kaumaya et al. do not specifically disclose making antibodies using the peptide of SEQ ID NO.5 and further testing the effect of the antibodies on cell proliferation, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make antibodies using the peptide of SEQ ID NO.5. One would have been motivated to do so because Kaumaya et al. explicitly teach that the peptide of SEQ ID NO.5 is HER2 B cell epitope and have the ability to induce production of antibodies that are immunoreactive with the extracellular domain of the HER2 protein. Moreover, one would have been motivate to make antibodies using the peptide of SEQ ID NO.5 and further test the effects of the antibodies on cell proliferation

for the purpose of identifying cancer drugs. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to make antibodies using the peptide of SEQ ID NO.5 because Kaumaya et al. teach how to immunize an animal with the HER2 B cell epitope and purify antibody from the animal sera. The antibodies made by the peptide of SEQ ID NO.5 will bind to the residues 247-268 of instant SEQ ID NO.1.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to HONG SANG whose telephone number is (571)272-8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Hong Sang/
Examiner, Art Unit 1643
6/16/08